

**NEURONAL CALCIUM SENSOR 1 AND PHOSPHATIDYLINOSITOL 4-OH KINASE-BETA INTERACT IN NEURONAL CELLS AND ARE TRANSLOCATED TO MEMBRANES DURING NUCLEOTIDE EVOKED EXOCYTOSIS**

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Neuronal Calcium Sensor-1 (NCS-1) belongs to a family of EF-hand calcium binding proteins and is mainly expressed in neurons and neuroendocrine cells where it causes facilitation of neurotransmitter release through unknown mechanisms. The yeast homologue of NCS-1 has been demonstrated to interact with and regulate the activity of yeast phosphatidylinositol 4-OH kinase-beta (PI4Kbeta). In neurons and neurosecretory cells, however, NCS-1 has not unequivocally been shown to interact with PI4Kbeta. Here we have compared the subcellular distribution of NCS-1 and PI4Kbeta and investigated whether they are capable to form complexes. In neurons, both proteins are widely distributed and are present in perikarya and, though to a lesser extent, in nerve terminals. A consistent portion of NCS-1 and PI4Kbeta is cytosolic, whereas a portion of both proteins appears to be associated with the membranes of the endoplasmic reticulum and the Golgi complex. Very small amounts of NCS-1 and PI4Kbeta are present in synaptic vesicles. Our results further demonstrate that in neurosecretory cells, endogenous NCS-1 and PI4Kbeta interact to form a complex which can be immunoprecipitated from membrane as well as from cytosolic fractions. Moreover, both proteins can be recruited to membranes when cells are treated with nucleotide receptor agonists known to increase polyphosphoinositide turnover and concomitantly induce exocytosis of secretory vesicles. These findings demonstrate that mammalian NCS-1 and PI4Kbeta interact under physiological conditions and suggest a possible role for NCS-1 in the translocation of PI4Kbeta to target membranes.